The effectiveness of interventions targeting physical activity and/or sedentary behaviour in people with Multiple Sclerosis: a systematic review

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Manuscript Title: The effectiveness of interventions targeting physical activity and/or sedentary behaviour in people with Multiple Sclerosis: a systematic review

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Declaration of Interest

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Abstract

Background: Remaining physically active is important to maintain functional ability and reduce the incidence of co-morbidities in people with Multiple Sclerosis. The aim of this review was to evaluate the effectiveness of interventions on physical activity or sedentary behaviour in people with Multiple Sclerosis.

Methods: A systematic search was conducted in May 2018 of the following databases: Web of Science Core Collections, Embase and Medline. Included studies were randomised controlled trials involving people with Multiple Sclerosis who completed an intervention, compared to any comparator. Outcomes included subjective or objective measures of physical activity or sedentary behaviour. Quality assessment was performed using the Physiotherapy Evidence Database scale.

Results: Twenty-five trials were included covering 1697 participants, the majority of which had mild-moderate disability (average Physiotherapy Evidence Database score 6.2±1.5). Experimental interventions included exercise prescription (n=5), behaviour change interventions (n=10), combined exercise and behaviour change techniques (n=7) and education (n=3). Generally, subjective but not objective physical activity improved in those with mild-moderate disability. Insufficient data existed on the effectiveness on sedentary behaviour.

Conclusion: A discrepancy seems to exists between the effectiveness of physical activity interventions in people with Multiple Sclerosis depending on whether physical activity was assessed objectively or subjectively, with the latter indicating effects. Effects on sedentary behaviour remain to be elucidated.

Keywords: Multiple Sclerosis, Physical Activity, Sedentary Behaviour, Measurement, Disability, Review.

Introduction

Multiple Sclerosis (MS) is a chronic progressive condition typically diagnosed when people are between 20 and 40 years old, and over time resulting in functional impairment and disability [1]. In people with MS, remaining physically active is important to maintain functional ability, independence, quality of life and to reduce the incidence of co-morbidity [2]. Nonetheless, people with MS often find engaging in physical activity and exercise challenging [3], and are less physically active than the general population [1,4]. Of particular concern, data suggests that only 20% of people with MS meet the recommended public health levels of Moderate-to-Vigorous Physical Activity (MVPA) compared with nearly 40% of healthy controls [5]. Furthermore, people with MS more frequently participate in sedentary activities, such as sitting or reclining that requires very low levels of energy (<1.5 Metabolic equivalent) [6,7].

Engaging in physical activity and reducing prolonged sedentary behaviour is important for reducing the impact of functional impairment, disease progression and depression [1,8,9]. From a health perspective low levels of physical activity and pronounced sedentary behaviour raise concerns due to the well-established associated risk of other conditions, such as cardiovascular diseases (CVD), hypertension and glucose intolerance [10]. Recent evidence has found that people with MS have a higher incidence rate of myocardial infarction, stroke and heart failure and an increased relative risk of CVD than matched controls, regardless of age and country of birth [11–13]. Furthermore, people with MS are ~2.5 times more likely to develop insulin resistance compared to healthy controls [14]. The reason for the increased risk of co-morbidity in MS, found across the disability spectrum (Expanded Disability Status Scale (EDSS) 0.5-6.0) is largely unknown [15], and may (in part) be explained by the common manifestations of MS and CVD, such as immune system dysfunction and inflammation, the use of disease modifying drugs and other MS treatments. However, it likely also relates to a lack of physical activity and a predominance of sedentary behaviour, leading to reduced insulin sensitivity and glucose tolerance and an increased risk of CVD [16,17].

Clearly, effective interventions that can assist people with MS to be more physically active are highly warranted. Such interventions typically focus on behaviour change,

the identification of barriers and facilitators and self-monitoring and/or engagement in exercise. Sangelaji et al. [18] recently conducted a systematic review of studies evaluating behaviour change interventions aiming to increase physical activity participation. This review included 19 studies, not all of which included a measure of PA, and found that behaviour change interventions, of relatively short duration (8-12 weeks) may increase physical activity participation. However, the review by Sangelaji et al. [18] did not report on the baseline and post-intervention physical activity levels, did not include measurement of sedentary behaviour, and did not explore the effectiveness of interventions according to disability level. This is of importance since people with greater disability are known to engage in less physical activity and the more disabled group may therefore react differently to interventions than those of milder disability levels [19]. Therefore, the aim of the current review was to evaluate the effectiveness of interventions which target physical activity or sedentary behaviour in people with MS and evaluate variables, such as disability level, disease type and measurement technique, which may influence effectiveness.

Methods

The present systematic review follows the PRISMA guidelines on systematic reviews of Randomised Controlled Trials (RCTs) [20]. No predefined review protocol was published. Specifically the following PICO question [21] was formulated: “Amongst people with MS, to what extent do interventions aiming to improve physical activity or reduce sedentary behaviour (according to the definition of Caspersen et al. [22] and Pate et al. [23]), in comparison to usual-care/wait-list control, active control or to another intervention, improve the level of physical activity or reduce sedentary behaviour evaluated by patient reported outcomes or accelerometry”.

Search strategy

An electronic search of the following electronic databases: Web of Science Core Collections, Embase and Medline was conducted in May 2018. No restrictions were placed on publication date, or type/length of intervention. The following keywords were used: (‘step count’ OR walk* OR pedometer OR accelerom* OR ‘physical fitness’ OR behavio* OR intervention OR sedentary OR sitting) OR (‘physical activity’ OR exercise) OR (‘International Physical Activity Questionnaire’ OR ‘Health Promoting Lifestyle Profile’ OR ‘Godin Leisure-Time Exercise Questionnaire’ OR

‘Physical Activity Scale for Individuals with Physical Disabilities’ OR ‘Physical Activity and Disability Survey-Revised’ OR ‘7-Day Physical Activity Recall’ OR ‘PhoneFITT’ OR ‘Rapid Assessment of Physical Activity’ OR ‘BAECKE’) AND (‘Multiple Sclerosis’). The reference lists of relevant articles were also searched.

Inclusion and exclusion criteria

To be included in the systematic review articles had to (i) include solely participants with MS or, where there was a combination of patient groups, the data pertaining to those with MS could be extracted; (ii) randomise participants to an experimental, control or active control condition; (iii) measure physical activity and/or sedentary behaviour using subjective or objective methods; (iv) be available in English. Articles were excluded if they were non-RCTs, non-human studies or conference abstracts. Search results were saved and exported to www.covidence.org where duplicates were removed. Articles were initially screened by title and abstract, and the full text of relevant articles were read by two reviewers (EC and SB). Data was extracted by one reviewer (EC) and checked for accuracy by a second reviewer (SB).

Quality assessment

Quality assessment (external validity, internal validity and the reporting of statistics) was assessed using the 11-item Physiotherapy Evidence Database (PEDro) scale which has been shown to be reliable and valid in rating the methodological quality of studies [24,25]. The scale gives a score out of ten (no point is awarded for the initial item of stating inclusion and exclusion criteria) as per the guidelines. A cut-off score of 5 is often used to distinguish between high and low quality studies [25]. PEDro scores of articles included on the PEDro database were utilised if available. Articles that did not have a score available were scored independently by two reviewers (EC & SB) and scores were agreed. When there was a discprepancy in scores, differences were resolved via discussion which included a third reviewer. When two or more articles were from the same trial but reporting different outcome measures they were combined and considered as a single study and PEDro scores of articles published from the same trial were averaged.

Within included studies, interventions consisting of prescribed exercise (aerobic, strengthening, stretching) were considered as exercise interventions, those based on

behaviour change theory or motivational interviewing were considered as behaviour change interventions, those consisting of education or advice were considered as education interventions. Any interventions that consisted of a combination of exercise, behaviour change or education were considered as such. Dropout rates of ≤5%, 6-19% and ≥20% were considered as low, moderate and high respectively in accordance with Fewtrell et al. (2008); and disability ranges of mild (EDSS 0-4.0, PDDS 0-3), moderate (EDSS 4.5-6.5, PDDS 4-6) and severe (EDSS ≥7.0, PDDS ≥7) were used to differentiate between people with MS with different levels of ambulatory dysfunction [27].

Results

Outcome of search

From the electronic search, 7412 articles were identified (Figure 1). From these 3225 duplicates were removed. Out of the remaining records reviewed by title and abstract, 3867 and 273 records were removed by title and abstract, respectively. Forty-seven articles were selected for full text review. Following this, 17 articles were excluded, resulting in 30 included articles for review. In three instances articles were published from the same study and were therefore combined. In total, 25 individual studies, published over 30 articles were included within this review (Figure 1). Full results of the PEDro scoring are reported in Table 1.

FIGURE 1 NEAR HERE

TABLE 1 NEAR HERE

Quality assessment and study characteristics

PEDro scores ranged from 3 to 8 out of 10, (mean score of 6.2 ± 1.5), with the majority of trials (n=21) obtaining a score of 5 out of 10 or more indicating higher quality (Table 1). Lower scores were mainly caused by lack of blinding of participants, therapists or assessors, and failing to conduct analyses with intention to treat where appropriate.

The included studies covered 25 RCTs described in 30 articles. A total of 1697 participants were included in the review with study samples ranging from 14 to 218 participants. Studies evaluated interventions based upon exercise prescription (n=5)

[28–32]; behaviour change interventions (n=10) [33–46]; exercise prescription and behaviour change interventions (n=7) [47–54]; and health promotion education (n=3) [55–57] (Table 2).

The length of interventions ranged from 1 week [33] to 6 months [29,37–40] (Table 2). The majority of studies (n=14) lasting 8-12 weeks [28,30,31,34,35,41–44,48–52,55,57]; with other interventions lasting four [47], five [56] and six months [29,37–40,46,54]. Thirteen studies did not follow-up participants after the intervention period, while 12 studies included a follow-up assessment of participants at 1 month [33]; 3 and 6 months [34,57], 6 months only [30,41–43,49,50], 8 months [56], 6 and 9 months [52,53], 9 months only [48] and 12 months [54].

TABLE 2 NEAR HERE

Dropout, adherence, adverse events

Dropout rates were low in seven studies [28,34–36,43,45,55]; moderate in 15 studies [29,31,33,41,42,44,46–54,56,57]; and high in two studies [30,32]. In one study, published over four articles [37–40] there were notable discrepancies in their reporting of 'non-completers' in one trial, published over four papers, with between 7 and 20% of participants not providing post-intervention data [37–40]. Adherence (measured via self-report, website log-ins, attendance to face-to-face/telephone/video conferencing sessions) to the intervention was reported to be 75% or greater in 14 studies [28,29,34–40,43,46–48,50,51,56,57], less than 75% in seven studies [30–32,44,45,52–54], while adherence was not reported in four studies [33,41,42,49,55]. Ten trials reported that no adverse events occurred [28,29,35,41–43,46,48,50,54,57], while three trials [32,47,52,53] reported mild adverse events (hip pain, spasticity, symptom exacerbation, increased fatigue). The remaining 12 trials did not report if any adverse events occurred [30,31,33,34,36–40,44,45,49,51,55,56] (Table 2). MS relapses were reported in three trials only [48,50,57], four trials reported no MS relapses [28,40,43,47], while the remaining 18 trials failed to report the occurrence of relapses [29–36,41,42,44–46,49,51–56].

Disability level and type of MS

Generally studies recruited participants with a range of disability levels. People with mild disability only were recruited in four trials [28,30,47,52]; moderate disability only in one trial [31] and severe disability only in one trial [35]. Participants with mild-moderate disability were recruited in 16 trials [29,33,34,36–46,48–50,54,57] (Table 2). People with mild, moderate and severe MS were recruited in one trial only [55] while disability severity was unknown in Plow et al. [51] and Stuifbergen et al. [56]. The majority of studies recruited participants with all types of MS (relapsing remitting, primary progressive, secondary progressive, benign) (n=16) [29–32,34,35,37–42,45–48,52–55,57], five studies recruited only participants with relapsing remitting MS [36,43,44,49,56], and four study did not report MS type [28,33,50,51] (Table 2).

The majority of trials (n=16) found positive results for physical activity outcomes following the intervention [28–31,33,34,36,41–45,48,49,54–56]. Four trials found inconclusive results between measurement methods reported within studies [32,37–39,46,47], while an additional four trials did not report improvements in physical activity compared to control after the intervention [35,50,51,57]. With regards to sedentary behaviour, there were only two trials, including those with mild-moderate disability, which reported sedentary behaviour as an outcome with conflicting results found between trials [29,40] (Table 2; Table 3).

TABLE 3 NEAR HERE

Intervention type and dosage

Behaviour change: Of the 10 behaviour change interventions five trials incorportated telephone support or counselling with face-to-face appointments [41,42,45] with optional exercise DVD and home-monitoring [34], newsletters [36] or wheelchair skills training [35]; four trials delivered the intervention via the internet [37–40,43,44,46] while only one trial delivered the intervention in small group sessions [33]. Six trials stated their interventions were based on Social Cognitive Theory (SCT) [35–40,43,44,46], while motivational interviewing was utilised by four trials [33,34,41,42,45]. The duration and number of sessions of interventions based on behaviour change tended to be poorly described in the included trials. Only four trials [33,34,41,42,45] fully reported the duration and number of sessions of their interventions lasting a total of 180 minutes (3hrs within 1 week) [33], 210-240

minutes (3.5-4hrs within 12 weeks) [45], 251 minutes (4.2hrs within 6 weeks) [34] and 310-330 minutes (5.2-5.5hrs within 12 weeks) [41,42], and all reported a positive impact on physical activity outcomes [33,34,41,42,45]. The remaining five trials provided insufficent information to calculate total duration [35–40,43,44,46] (Table 2).

Exercise: Of the five exercise intervention trials, programmes were delivered within a gym environment [28,32] via DVD [29], the internet [30] or within a group format [31]. Exercise programmes tended to be poorly described with three trials providing insufficent information on the duration and/or number of exercise sessions [28–30]. The remaining two trials prescribed exercise interventions of between 600 minutes (10 hours within 4 weeks) [32] and 1440 minutes (24 hours within 12 weeks) [31]. Mostert and Kesselring [32] found improvements in sport physical activity, while no change was found in work or leisure physical activity, conversely Learmonth et al. [31] found a significant improvement in total physical activity. Interventions in all but one trial [32] lasted 12 weeks or more. From these results it appears that the higher the duration of exercise performed the more likely participants will increase their physical activity.

Combined exercise and behaviour change: Of the seven trials which combined exercise prescribed with behaviour change techniques, interventions were delivered within supervised and/or home exercise sessions [48–51], group-based [52,53], DVD [47] or Nintendo Wii [54] with additional face to face, telephone support, newsletters/leaflets or group discussion to facilitate behaviour change. Two trials provided sufficent information on the duration and/or number of sessions. Plow et al. [49] incorportated a combined exercise programme, 3-5 days per week for 30-45 minutes per session with customised leaflets. As such the total duration of exercise performed varied greatly between 18 and 45 hours (over 12 weeks). Carter et al. [48] incorportated a combined exercise programme, conducted at home and supervised, (1 hour/session, 3 days/week) lasting approximately 2160 minutes (36 hours over 12 weeks) with cognitive-behavioural elements within exercise sessions. Both trials reported improvements in physical activity [48,49]. While a moderate effect size was found in physical activity by Thomas et al. [54] in which a personalised exercise Nintendo Wii programme was incorporated with telephone and face-to-face contact over six months (duration and number of sessions per week unknown). Conversely,

four trials found no or inconsistent findings for improvements in physical activity [47,50–52]. Learmonth et al. [47] incorporated an individualised combined exercise programme, 4 sessions per week for 4 months (duration of sessions not provided), with newsletters and skype calls. This trial found inconsistent findings for improvements in physical activity. Carter et al. [50] incorporated 3 hourly sessions/week over a 10 week period, lasting a total of 30 hours, with no significant improvements in physical activity. Plow et al [51] reported the home exercise programme provided to participants (45 minutes/session, 5 days/wk), but failed to report sufficent information on the duration of four physical therapy sessions (group 1) and telephone support (groups 1 and 2) provided over aneight week period, with no improvements in physical activity; and finally, Coote et al. [52] incorporated group and home-based exercise at the current MS physical activity guidelines [58] for 10 weeks; supplemented by coaching phone calls and SCT-based group discussion with no improvements in physical activity (table 2; Table 3).

Education: Three trials consisted of education interventions utilising groups sessions in which health promotion topics were discussed. Ennis et al. [55] reported weekly sessions lasting 3 hours over 8 weeks, a total duration of 24 hours and Stuifbergen et al. [56] reported weekly sessions which lasted 90 mins over 8 weeks (a total duration of 12 hours) with additional bimonthly telephone support (duration of telephone calls not reported). Both trials reported improvements in physical activity. Conversely, Hugos et al. [57] incorporated DVD viewing with group discussion during weekly sessions lasting 2 hours over 6 weeks (total duration 12 hours) with no improvements found in physical activity.

Outcome

Physical activity or sedentary behaviour were reported as the primary outcome measure in seven trials only [36,43,44,46–49]. Participation in physical activity and sedentary behaviour was measured using a range of outcome measures, with some trials measuring physical activity and/or sedentary behaviour using more than one outcome measure. Only six studies used objective methods to measure physical activity, using the actigraph (GT3X, GT2M, GT3X+) [35,37,38,46–48] and SenseWear armband [52]. The most commonly used subjective measurement tools to measure physical activity were the Godin Leisure-Time Exercise Questionnaire

(GLTEQ) (n=13) [29,34,36–38,43,44,46–50,52,54]; Health Promoting Lifestyle Profile II (HPLP-II), which includes a physical activity subscale, (n=5) [33,45,51,55,56], and BAECKE questionnaire (n=2) [30,32]. The Physical Activity Scale for Individuals with Physical Disabilies (PASID), International Physical Activity Questionnaire (IPAQ), Physical Activity and Disability Survey-revised (PADS-r), 7-day Physical Activity Recall (7-Day PAR), PhoneFITT questionnaire and Rapid Assessment of Physical Activity questionnaires were all used in one trial each [28,31,39,41,42,49,57]. Sedentary behaviour was measured in two trials and in both cases using subjective methods; Sitting Time Questionnaire [29] and IPAQ [40].

Characteristic/feature of Physical Activity or Sedentary Behaviour

Total Physical Activity

A total of 12 trials (reported over 13 articles) investigated total physical activity [28,31,33,35,39,41,42,45,49,51,52,55,56]. The majority of trials (n=10) reported significant improvements in total physical activity with either time or time x group effects reported [28,31,33,34,39,41,42,45,49,51,55,56]. Improvements in physical activity remained significant at follow-up in four out of five trials that included a follow-up assessment [33,49,51,56] (Table 3). Interventions that reported significant improvements consisted of behaviour change interventions (n=4) [33,39,41,42,45], exercise (n=2) [28,31], exercise and behaviour change interventions (n=2) [49,51], and education (n=2) [55,56]. Two trials reported no change in total physical activity, these studies consisted of combined exercise and behaviour change and behaviour change only in people with mild [52] and severe disability [35] measuring physical activity objectively using the SenseWear armband and actigraph respectively (Table 3).

Compared to control or active control groups, total physical activity improved by an average of 39% (SD 28%) between baseline and post-intervention, with one outlier removed which reported physical activity of the intervention group to increase six fold compared to the control group [49]. Plow et al. [51] and Bombardier et al. [45] reported effect sizes or change scores only, as such percentage change could not be calculated (Table 3).

Leisure-time Physical Activity

A total of 13 trials (reported over 14 articles) investigated leisure physical activity [29,32,34,36–38,43,44,46–50,52]. The majority of studies (n=10) found significant improvements in leisure-time physical activity [29,34,36–38,43,44,46–48].while three trials reported no improvement [32,50,52] (Table 3). Improvements in leisure-time physical activity remained significant at follow-up in three out of six trials that included a follow-up assessment [34,43,49] (Table 3). While Coote et al. [52] reported significant within group improvments at post-intervention and at three and six month follow-up these improvements were not significant compared to the active control group (Table 3). Significant improvements were reported across interventions of behaviour change (n=6) [34,36–38,43,44,46], exercise prescription (n=1) [29] and combined exercise and behaviour change (n=3) [47–49]. Compared to control or active control groups leisure-time physical activity improved by an average of 79% (SD 29%) between baseline and post-intervention (Table 3).

Moderate-Vigorous Physical Activity

Four trials investigated MVPA [29,37,46,47], of which only one found significant improvements in MVPA [29] (Table 3). McAuley et al. [29] investigated a six month home-based DVD exercise intervention. The remaining three trials consisted of a four month combined exercise and behaviour change intervention (n=1) [47] and a six month internet behaviour change intervention (n=2) [37,46] (Table 2). Learmonth et al. [47], Pilutti et al. [37] and Motl et al. [46] all measured MVPA objectively using the actigraph accelerometer and therefore were not subject to issues with memory recall. No studies included follow-up assessments.

Steps taken

Two trials investigated steps taken per day [48,52], both of which investigated the effects of combined exercise and behaviour change interventions. A significant improvement of 689 steps/day was found by Carter et al. [48], however this improvement was not maintained at 9 month follow-up (Table 2; Table 3). While Coote et al. [52] found no within or between group difference in steps taken at post-intervention and at three and six month follow-up (Table 3).

Sitting time

Two trials investigated sedentary behaviour [29,40]. Klaren et al. [40] reported

significant improvements in sedentary behaviour following a six month internet behaviour change intervention; while McAuley et al. [29] reported no change in weekday or weekend sitting time following six months of an exercise intervention (Table 2; Table 3). No follow-up assessments were conducted in either trial. Both trials employed subjective methods to measure sedentary behaviour. While significant improvements were reported by Klaren et al. [40] there were large differences in sitting time at baseline between groups (intervention group- 550(±223) mins/day, control group- 412(±193) mins/day).

Other outcomes

Three trials investigated other physical activity outcomes. Tallner et al. [30] reported a significant improvement in Sport physical activity after three months of an internet-based exercise intervention, yet this improvement was not maintained at six month follow-up. A significant improvement was also reported in sport physical activity, while no improvement was reported in Work physical activity conducted by Mostert and Kesselring [32] following a four week exercise intervention (Table 3). Finally, Hugos et al. [57] reported no improvement in the frequency of cardiovasular, strengthening and flexibility exercise performed by participants after a six week fatigue education intervention (Table 2; Table 3).

Discussion

The findings of this review indicate that interventions consisting of behaviour change, exercise prescription, combined exercise and behaviour change and health promotion education appear to subjectively infuence physical activity, whereas objectively assessed physical activity is less likely to change if at all. With regards to sedentary behaviour there is inadequate evidence to determine the effects of these interventions. Despite the overall acceptable methodological quality of the included trials (6.1 ± 1.5), studies should be interpreted with caution as four trials obtained a score of less than 5/10 [25], and since physical activity or sedentary behaviour was a primary outcome in only seven trials studies may be inadequately powered to detect a significant change.

Interventions were heterogeneous in type, dosage, frequency and duration. It is not clear whether certain interventions were superior to others or whether a certain

intervention dosage, frequency or duration is optimal to positively influence physical activity or sedentary behaviour. The majority (n=10) of interventions lasted 12 weeks, regardless of intervention type, and it appears that the longer the intervention and more engaged participants are then the more likely they will increase their physical activity. Many studies did not provide sufficient information on the content of the intervention and duration of sessions. Therefore, it was not possible to calculate exact intervention dosage, replicate interventions in clinical practice or assess the effectiveness of interventions on MS type or disability level. Studies tended to include participants who were of mild or mild-moderate levels of disability. Moreover, no studies compared the effects of interventions across disability levels, which may influence the effectiveness substantially. While Ennis et al. [55] recruited across all disability levels the effects of the intervention between disability levels was not explored.

Heterogeneity was also present in measurement technique and aspect of physical activity of interest. Where commonality existed between trials in outcome and unit of measurement it was possible to establish some meaningful outcomes for physical activity and sedentary behaviour across studies. At baseline, participants accumulated an average of 15(SD 8) minutes of MVPA/day (n=4), 5,626(SD 1,283) steps/day (n=2), 17.2(2.3) MET/week (n=2), 13.8(SD 1.8) MET/min/week (n=2), and 614(SD 111) minutes sitting/day (n=2). These physical activity and sedentary behaviour levels are similar to those reported in previous MS literature [59,60]. However, within these trials participants were not meeting the disease-specific physical activity guidelines prior to, or following the intervention [58].

In general, studies which reported subjective physical activity found significant improvements. Six trials used objective measurement tools to assess the effects interventions had on physical activity of which only one [48] reported significant improvements. Only two studies reported sedentary behaviour, finding conflicting results [29,40], both of which utilised subjective methods. The reasons for the discrepancies between objective and subjective measures remain unclear. It is well recognised that self-report questionnaires are limited in their validity due to issues such as memory recall, social desirability and are subject to overestimation, particularly in inactive populations [61]. In addition, these measurement tools are

potentially measuring different aspects of physical activity or periods of time particularly if participants complete a retrospective self-report questionnaire prior to attaching an activity monitor to objectively and prospectively measure physical activity. Self-report tools can vary in the recall period the respondent has to consider, such as previous day/week; while some, such as the Godin Leisure-Time Exercise Questionnaire, are unanchored, asking participants to recall a typical week. Crucially, some of the questionnaires (Physical Activity and Disability Survey-revised, PhoneFITT, BAECKE, Rapid Assessment of Physical Activity) have not been validated in people with MS. Other questionnaires were found to have only modest criterion validity with objective measures such as accelerometers; Godin Leisure-Time Exercise Questionnaire (r=0.53) [62]; (r=0.52) [63]; Physical Activity Scale for Individuals with Physical Disabilies (r=0.22-0.37); International Physical Activity Questionnaire (r=0.36) [62]; and 7-day Physical Activity Recall (r=0.75) [63]. In particular, the Physical Activity Scale for Individuals with Physical Disabilies has been found to overestimate physical activity by an average of 2.4 hours/day in people with physical disabilities [64]. As such, results which rely solely on self-reported physical activity should be interpreted with caution [64,65]. Similar to physical activity, sedentary behaviour cannot be accurately determined by self-report questionnaire since differences of 2-4 hours/day can exist between self-report questionnaires and objectively measured sedentary behaviour [66], and reported differences should be interpreted with caution [67]. Therefore, objective measurement tools which have been validated for the measurement of sedentary behaviour should be utilised in future.

The results of this review are in agreement with a review by Sangelaji et al. [18] of 19 studies exploring the effects of behaviour change techniques on participation in physical activity in MS of which 11 out of 25 trials were included in the current review. The current review adds novel findings from the inclusion of different interventions, measurement techniques and sedentary behaviour. The results of this review are similar to a previous findings in stroke and acquired brain injury which have indicated that there is some/limited evidence for increasing physical activity [68,69]. With respect to sedentary behaviour there is some evidence interventions can reduce sedentary behaviour in healthy adults by 22 minutes/day yet the majority of included studies used self-report [70]. The findings of this review are in agreement

with a recent review by Casey et al. [71] which included 14 trials which found physical activity interventions improve subjective but not objective physical activity in people with MS.

This systematic review has a number of limitations. Firstly, only RCTs were included. While RCTs are among the highest levels of evidence due to their reduced risk of bias, this review did not consider high quality cohort or case-controlled studies. Included studies were further limited to English language; as a result, language bias may be present. Finally, this review is limited in its generalisability in that the included studies mainly represented people with mild-moderate disability. Included studies varied in the construct of physical activity measured including total physical activity, MVPA, leisure, sport and work physical activity, counts, minutes, energy expenditure and steps taken as well as various units of measurement therefore making comparisons between studies difficult.

The present study identified several aspects that need further investigation. First, well-powered studies that utilise a valid assessment of physical activity or sedentary behaviour in studies where these are the primary outcome, are warranted. Second, more advanced (gold standard) physical activity outcomes such as the double-labelled water method would greatly strengthen future studies [72]. Third, studies comparing relevant and well-described interventions head to head are lacking in the literature. Fourth, interventions that target physical activity or sedentary behaviour in more disabled persons with MS are needed.

Conclusion

Exercise prescription, behaviour change interventions, combined exercise and behaviour change interventions and health promotion education appear to subjectively improve physical activity in people with MS with mild-moderate disability; however, this most often is not the case when physical activity is assessed objectively, but further confirmation is needed. Furthermore, there is a lack of evidence to support the effectiveness of these interventions on sedentary behaviour.

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Figure 1. PRISMA flowchart of screening and inclusion process of included trials.

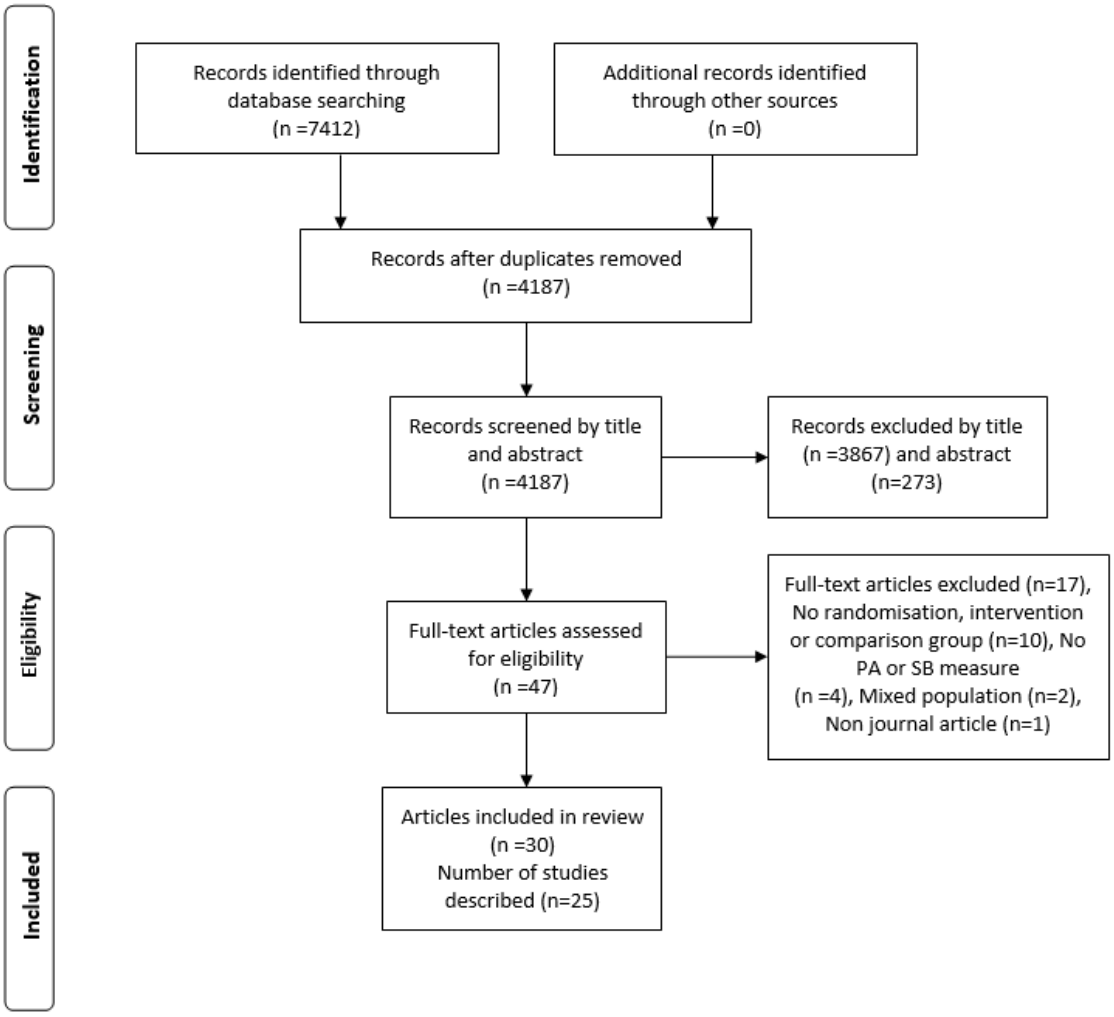

Table 1. PEDro scores for included randomised controlled studies.

Author	Eligibility Criteria*	Random allocation	Concealed allocation	Baseline comparability	Participant blinding	Therapist blinding	Assessor blinding	<15% DO	ITT	Between-group difference	Point Estimate and Variability	Total (0-10)
Thomas et al [54]	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Motl et al [46]	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Hugos et al [58]	Y	Y	Y	Y	Y	N	N	Y	Y	Y	Y	8
Coote et al [52] ¥	Y	Y	Y	Y	Y	N	Y	N	N	Y	Y	7
Hayes et al [53] ¥	Y	Y	N	Y	N	N	Y	N	Y	Y	Y	6
Learmonth et al [46]	Y	Y	Y	Y	N	N	N	Y	N	Y	Y	6
Dashti et al [33]	Y	Y	Y	Y	N	N	N	N	N	Y	Y	5
Tallner et al [30]	Y	Y	Y	Y	N	N	Y	Y	N	Y	Y	7
Turner et al [34]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
McAuley et al [29]	Y	Y	N	Y	N	N	Y	Y	Y	Y	Y	7
Rice et al [35]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5
Suh et al [36]	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Wens et al [28]	N	Y	Y	Y	N	N	N	Y	N	Y	Y	6
Carter et al [47]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Pilutti et al [37] †	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5
Pilutti et al [38] †	Y	Y	Y	Y	N	N	N	Y	N	Y	Y	6
Sandroff et al [39]†	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5
Klaren et al [40]†	Y	Y	Y	Y	N	N	N	N	Y	Y	Y	6
Carter et al [49]	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8
Plow et al [48]	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Bombardier et al [42] §	Y	Y	N	Y	N	N	N	Y	N	N	Y	4
Kratz et al [41]§	Y	Y	N	Y	N	N	N	Y	N	N	Y	4
Dlugonski et al [43]	Y	Y	N	Y	N	N	N	Y	Y	Y	Y	6
Learmonth et al 2012	Y	Y	N	Y	N	N	Y	Y	Y	Y	Y	7
Motl et al [44]	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	7
Plow et al [50]	Y	Y	N	N	N	N	Y	N	N	Y	N	3
Bombardier et al [45]	Y	Y	Y	N	N	N	Y	Y	Y	Y	Y	7
Ennis et al [51]	Y	Y	N	Y	N	N	N	Y	N	Y	Y	5
Stuifbergen et al [52]	Y	Y	N	Y	N	N	N	N	N	Y	Y	4
Mostert & Kesselring [32]	Y	Y	N	Y	N	N	N	N	N	N	Y	3

Abbreviations: DO: Dropout; ITT: Intention To Treat.

All PEDro scores obtained from PEDro online database except Hugos et al (2017) and Dashti et al (2016) which were scored by EC and SB.

† Articles published describing the same trial.

§ Articles published describing the same trial.

¥ Articles published describing the same trial.

Table 2. Study characteristics of included randomised controlled studies.

Study	Intervention modality	Sample size, age	Drop-outs, adherence, adverse events, MS relapses	Disability level, MS type	Duration/Frequency (sessions/week)	Intervention regime
Thomas et al. 2017 [54]	EXP: Nintendo Wii home-exercise with behaviour change strategies CON: Waitlist control	n=30 EXP=15 50.9(8.1) years CON=15 47.6(9.3) years	DO 2/30 (7%) Adherence 31% No Adverse events MS relapses NR	APDDS 2-6 MS Type all	6 months Individualised programme prescribed	Week 1 & 2: face-to-face appointment, orientation to Wii Week 3: Install equipment and commencement of individual programme at home Week 5: follow-up by telephone/email Week 7: home visit Week 12 & 16: follow-up by telephone/email Week 20-26: Monthly telephone/email support
Motl et al. 2017 [46]	EXP: Internet delivered behaviour change based on SCT CON: Waitlist control	n=47 EXP=23 52.3(10.3) years CON=24 51.4(7.4) years	DO 4/47 (9%) Adherence 97% No Adverse events MS relapses NR	PDDS 2.0* (IQR 3.0) MS Type all	6 months Months 1/2- 7 website sessions, 7 video sessions Months 3/4- 4 website sessions, 6 video sessions Months 5/6- 2 website sessions, 2 video sessions	Website content incorporating SCT. 15 video coaching sessions. Pedometer to self-monitor daily step counts

Hugos et al. 2017 [57]	EXP: Group-based fatigue education CON: Group-based MS education	n=218 EXP=109 53.9(9.8) years CON=109 53.6(10.5) years	DO 14/218 (6%) Adherence 91% No Adverse events MS relapses EXP 4/109 CON 4/109	EXP EDSS 5.1(1.1) CON EDSS 5.3(1.1) MS Type all	6 weeks 1 session/week, 2 hours	DVD viewing, group discussion, individual goal setting. Topics included: managing depression, sleep disturbance, heat sensitivity, deconditioning, setting priorities and goals, managing mobility problems, energy conservation and exercise.
Hayes et al. 2017 [53]	EXP: Group exercise and SCT behaviour change A-CON: Group exercise and attention control education	n=65 EXP=33 42.3(9.9) years A-CON=32 41.9(9.3) years	EXP DO 4/33 (13%) CON DO 3/32 (9%) Adherence EXP 68% CON 50% Adverse events 1/65 in CON MS relapses NR	PDDS 0-3 MS Type all	10 weeks aerobic training 2 sessions/week, 10-30 minutes, strength training, 2 sessions/week, and group discussion	Group and home-based exercise consisting of aerobic (progressed to meet 30 minutes, moderate intensity) and strengthening exercise (progressed to 12 repetitions x 2 sets of each exercise), and 4 telephone coaching calls. SCT topics: self-efficacy, outcome expectations, goal-setting, barriers and benefits
Coote et al 2017 [52]	EXP: Group exercise and SCT behaviour change A-CON: Group exercise and attention control education	n=65 EXP=33 42.3(9.9) years A-CON=32 41.9(9.3) years	EXP DO 4/33 (13%) CON DO 3/32 (9%) Adherence EXP 68% CON 50% Adverse events 1/65 in CON MS relapses NR	PDDS 0-3 MS Type all	10 weeks aerobic training 2 sessions/week, 10-30 minutes, strength training, 2 sessions/week, and group discussion	Group and home-based exercise consisting of aerobic (progressed to meet 30 minutes, moderate intensity) and strengthening exercise (progressed to 12 repetitions x 2 sets of each exercise), and 4 telephone coaching calls. SCT topics: self-efficacy, outcome expectations, goal-setting, barriers and benefits

Hayes et al. 2017 [53]	As above	As above	As above	As above	As above	As above
Learmonth et al. 2017 [47]	EXP: DVD exercise and SCT newsletters & skype calls CON: Waitlist control	n=57 EXP= 29 48.7(10.4) years CON= 28 48.2(9.1) years	EXP DO 4/29 (14%) CON DO 2/28 (7%) Adherence 90% Adverse events 2/29 No MS relapses	PDDS ≤ 3.0 MS Type RR 98%	4 months aerobic training 2 sessions/week, 10-30 minutes strength training 2 sessions/week	Individualised programme consisting of aerobic exercise (walking at moderate intensity with pedometer to self-monitor), strength training (LL, UL, core), 1-2 sets, 10-15 repetitions of 10 exercises on DVD. 6 newsletters based on SCT and skype call in weeks 2, 4, 6, 9, 12 & 15.
Dashti et al. 2016 [33]	EXP: Motivational interviewing CON: Group discussion about the disease	n=60 EXP= 26 31.8(7.4) years CON=25 30.4(6.2) years	EXP DO 4/30 (13%) CON DO 5/30 (17%) Adherence NR Adverse events NR MS relapses NR	EDSS 0-5.5 EXP 1.69±1.3 CON 1.48±1.02 MS Type NR	1 week 3 sessions/week, 1 hour	Small groups (n=10) 1st session: norms, process of group, effects of behaviour, alteration stages, evaluation of commitment and trust, clarification opportunity 2nd session: positive/negative aspects of behaviour and change, human values, identification, clarification & confirmation of values 3rd session: perspective, recognition of tempting & helpful situations, evaluation of purpose, commitment, trust and motivation to change

Tallner et al. 2016 [30]	EXP: Internet-based exercise CON: Waitlist control	n=126 EXP= 59 40.9(10.4) years CON= 67 40.7(9.5) years	EXP DO 23/59 (39%) CON DO 26/67 (39%) Adherence 73% Adverse events NR MS relapses NR	EDSS ≤ 4.0 EXP 2.8(0.8) CON 2.7(0.8) MS Type RRMS, SPMS	3 months 3 sessions/week	Internet-based individuals exercise programme, 1 aerobic (10-60 minutes) and 2 strength training sessions/week, 2-3 sets/exercise, 1-2 minutes rest, BRPE 11-16. Email/telephone contact as required
Turner et al. 2016 [34]	EXP: Telephone counselling and home-based monitoring with optional exercise DVD A-CON: PA Education DVD	n=64 EXP=31 52.7(11.6) years A-CON=31 53.6(13.1) years Total sample 53.1(12.3) years	EXP DO 1/31(3%) A-CON DO 0/30 (0%) Adherence 99.5% Adverse events NR MS relapses NR	EXP MPS 2.35(1.50) A-CON MPS 2.73(1.35) MS Type all	6 weeks 1 session/week, Average telephone call- 41.8 minutes	DVD and brochure- benefits of PA for MS Motivational interviewing Telephone call, telehealth monitoring through phone to receive/deliver information using store and forward technology
McAuley et al. 2015 [29]	EXP: DVD exercise and telephone advice A-CON: healthy ageing DVD and telephone advice	n=48 EXP=24 59.6(1.4) years A-CON=24 59.8(1.5) years	EXP DO 2/24 (8%) A-CON DO 0/24 (0%) Adherence 100% No adverse events MS Relapses NR	EDSS <6.5 MS Type All	6 months, 3 sessions/week	11-12 exercises x 2 sets (balance, strength, flexibility). Exercises progressed every 2 weeks from 8-10 reps at RPE 10-12 (fairly light) to 10-12 reps at RPE 13-15 (somewhat hard). Exercise sessions progressed every 4 weeks. Telephone calls biweekly for 2 months with exercise tips then monthly for 4 months

Rice et al. 2015 [35]	EXP: SCT based behaviour change with custom-fit ultralight manual wheelchair, training and support CON: Usual care	n=14 EXP=9 53.3(11.1) years CON=5 54(0.4) years	DO 0% 89% Adherence No adverse events MS relapses NR	PDDS 7 MS Type All	12 weeks Telephone calls 1/week	Provided with custom-fit ultra-light wheelchair and technique/safety training. PA Behavioural intervention based on SCT via telephone
Suh et al. 2015 [36]	EXP: SCT based behaviour change via newsletters and telephone CON: Health and well-being newsletter	n=68 EXP=34 A-CON=34	EXP DO 1/34 (3%) A-CON DO 1/34 (3%) Adherence EXP 90.4% telephone calls completed A-CON 85.4% telephone calls completed Adverse events NR MS relapses NR	PDDS 2.0(1.8) MS Type RRMS	6 weeks Weekly newsletter and telephone calls (15 min)	Pedometer, logbook, newsletter topics: 1: benefits of PA 2: goal-setting for PA 3: how to improve exercise self-efficacy 4: outcome expectations 5/6: barriers/facilitators to PA Semi-structured phone interviews included goal-setting/monitoring step counts with pedometer
Wens et al. 2015 [28]	IT: High Intensity training and resistance training CT: Continuous training and resistance training CON: sedentary control	n=34 IT= 12 43(3) years CT=11 47(3) years CON=11 47(3) years	DO 0% 90% adherence to both exercise groups No adverse events No MS relapses	IT EDSS 2.3±03 CT EDSS 2.7±0.3 CON EDSS 2.5±0.3	12 weeks 5 sessions per 2 weeks	IT- warm up: 5 minute cycle Interval cycle training- week 1-6: Progressed from 5x1 minute cycle with 1 minute rest to 5x2 minute cycle with 1 minute rest at 80-90% max HR; week 6-12: 5x2 minute cycle with 1 minute rest at 90-100% max HR Resistance training- 1x10 RM to 2x20 RM of leg press, leg curl, leg extension, vertical traction, arm curl and chest press CT- Continuous cardio- cycle, treadmill walking/running from 1x6 minute/session to 2x1 0minute/session at 80-90% max HR

						Resistance training- as above
Carter et al. 2014 [48]	EXP: Supervised and home exercise and behaviour change techniques CON: Usual care	n=120 EXP =60, 45.7(9.1) years, CON =60, 46.0(8.4) years	EXP DO 6/60 (10%) CON DO 7/60 (12%) 9 months EXP DO 5/54 (9%) CON DO 3/53 (6%) Adherence: overall 86% (weeks 1-6 90%, weeks 7-12 81%) No adverse events MS relapses EXP= 10 relapses in 9 pwMS CON= 16 relapses in 14 pwMS	EXP EDSS 3.8±1.5 CON EDSS 3.8±1.5 MS Type All	12 weeks 1 hour, 3 sessions/week	Week 1-6: 2 supervised & 1 home sessions Week 7-12: 1 supervised & 2 home sessions with ET and/or RT ET: 5 x 3 minute, 2 minute rest, (e.g. stepper, cycle, treadmill, rowing, arm cranking, walking, swimming; gardening) at 50-60% of predicted max HR or 12-14 on BRPE RT: 5-20 repetitions x 1-3 sets, (e.g. wall press-ups, arm curls, leg abduction, squats/wall squats, knee extension, calf raises, sit-to-stand) BT: balance board, balance exercises, exercise ball work included (as appropriate) S: static stretching (as appropriate)

Pilutti et al. 2014 [37]	EXP: Internet delivered behaviour change based on SCT CON: Wait-list control	n=82 EXP=41, 48.4(9.1) years CON=41, 49.5(9.2) years	EXP DO 4/41 (10%) CON DO 2/41 (5%) Adherence NR Adverse events NR MS relapses NR	PDDS 3.0* (IQR 3.0) MS Type All	6 months Months 1/2- 7 website sessions, 7 video sessions Months 3/4- 4 website sessions, 6 video sessions Months 5/6- 2 website sessions, 2 video sessions	Website content incorporating SCT. 15 video coaching sessions. Pedometer to self-monitor daily step counts
Pilutti et al. 2014 [38]	As above	As above	EXP DO 6/41 (15%) CON DO 4/41 (10%) Adherence NR Adverse events NR MS relapses NR	As above	As above	As above
Sandroff et al. 2014 [39]	As above	As above	EXP DO 4/41 (10%) CON DO 2/41 (5%) Overall adherence 86% Adverse events NR MS relapses NR	PDDS 0-6 MS Type All	As above	As above
Klaren et al. 2014 [40]	As above	n=70 EXP=33 49.4(9.2) years CON=37 50.3(9.1) years	DO 14/70 (20%) Adherence NR Adverse events NR No MS relapses	PDDS EXP=2.0(3.0) CON=3.0(3.0) MS Type all	As above	As above

Plow et al. 2014 [49]	EXP: Home exercise program with customised leaflets CON: Waitlist control	n=30 EXP=14 47(9) years CON=16 48(10) years	EXP DO 2/14 (14%) CON DO 3/16 (18%) Adherence NR Adverse events NR MS relapses NR	EXP PDDS 1.5* CON PDDS 3.5* MS Type RRMS only	12 weeks	Exercise program prescribed in 2 x one-to-one sessions, consisting of indoor cycling, stretching, balance, strength training, 30-45 minutes, 3-5/week. Customised leaflets provided every 3 weeks for 24 weeks
Bombardier et al. 2013 [42]	EXP: PA counselling CON: Waitlist control	n=92 EXP=44 47.1(8.9) years CON=48 49.7(7.9) years	EXP DO 2/44 (5%) CON DO 9/48 (19%) 6 months EXP DO 6/42 (14%) Adherence NR No Adverse events MS relapses NR	EDSS ≤5.5 MS Type All	12 weeks	Motivational Interviewing to set goals to increase PA via face-to-face (40-60 minutes), 7 telephone counselling calls at weeks 1-4, 6, 8, 10 (30 minutes/call), 1 final face-to-face (60 minutes)
Kratz et al. 2014 [41]	As above	As above	As above	EDSS 4.0-6.5 MS Type All	As above	As above

Carter et al. 2013 [50]	EXP: Supervised and home exercise and behaviour change techniques CON: Usual care	n=28 EXP= 15 39.5(6.5) years CON= 13 40.9(8.7) years	EXP DO 1/15 (7%) CON DO 1/13 (8%) Adherence: 76% completed supervised exercise, 75% completed home exercise MS relapse EXP= 0 CON= 1	EDSS EXP= 3.0(1.1) CON=3.1(1.7) MS Type NR	10 weeks 1 hour, 3 sessions/week	2 supervised & 1 home sessions individualised programme consisting of aerobic (e.g. rowing, walking, cycling, cross-trainer), 5 x 3 minute, 2 minute rest at 50-69% of predicted max HR or 11-13 BRPE, balance, strength (e.g. squats, core stability) and flexibility (static stretches) exercise and Transtheorectical Model
Dlugonski et al. 2012 [43]	EXP: Internet delivered behaviour change based on SCT CON: Waitlist control	n=45 EXP =22 CON =23 46.6(9.7) years	EXP DO 0/22 (0%) CON DO 1/23 (4%) Adherence: website log ins on 10(2.7) out of 12 weeks, 73% logged in ≥10 weeks, attended 6.8(0.4) of the 7 video coaching sessions No adverse events No MS relapses	PDDS 1.0*[0-6] MS Type RRMS	12 weeks	Website and CD delivering text and video coaching incorporating SCT. 7 video coaching sessions delivered (5-10 minutes). Pedometer and pedometer log-book to self-monitor daily step counts
Learmonth et al. 2012 [31]	EXP: Group exercise CON: Usual care	n=32 EXP=20 51.4(8.1) years CON=12 51.8(0.5) years	8 weeks EXP DO 2/20 (10%) CON DO 1/12 (8%) 12 weeks EXP DO 1/18 (6%) CON DO 0/11 (0%)	EXP EDSS 6.14±0.36 CON EDSS 5.82±0.51 MS Type All	12 weeks 60 minute, 2/week	10 minute warm up (aerobic, stretching), 30-40 minute circuit exercise (1 minute of 8-12 of aerobic, resistance, balance exercises 1 minute rest between exercises), 5-10 minute cool down (aerobic, stretching, relaxation)

			Adherence 71% Adverse events NR MS relapses NR			
Motl et al. 2011 [44]	EXP: Internet delivered behaviour change based on SCT CON: Waitlist control	n=54 women only EXP =27 46.1(10.4) years CON =27 45.6(9.2) years	EXP DO 4/27 (15%) CON DO 2/27 (7%) Adherence: 71(15)% participants logged on per week, participants logged in on 8.6(3.0) of the 12 weeks Adverse events NR MS relapses NR	EXP PDDS 2.0(1.8) CON PDDS 2.1(1.9) MS Type RRMS	12 weeks Month 1: 4/month Month 2: 2/month Month 3: 1/month	Website delivering text and videos incorporating SCT. Chat sessions twice/week on online forum. Pedometer to self-monitor daily step counts
Plow et al. 2009 [51]	EXP1: Individualised physical rehabilitation EXP2: Group wellness rehabilitation	n=50 EXP1= 22 48.5(12.3) years EXP2= 20 48.5(9.1) years n=8 excluded from analysis (did not receive either intervention)	EXP1 DO NR EXP2 DO NR Adherence EXP1 95% attended all sessions EXP2 80% attended all sessions Adverse events NR MS relapses NR	MSFCϒ EXP1 0.1(0.6) EXP2 -0.02(0.7) MS Type NR	8 weeks EXP1: 4 physical therapy sessions, every 2 weeks, telephone support between sessions, 2 adherence telephone calls post-intervention EXP2: 2 hours/session, 7 weekly sessions, 2 adherence telephone calls post-intervention.	EXP1: Assessed strength, gait and flexibility. Home exercise program prescribed in 2nd session (indoor bicycling, stretching 3 days/week, strength and balance 2 days/week, 45 minutes/session) EXP2: Session topics covered: maximising health with MS, promoting PA, setting health goals and prescribing exercise programs, nutrition, stress and depression, energy conservation, priority setting. Home exercise program prescribed as EXP1 in 3rd session

					Telephone summary for those who missed sessions	
Bombardier et al. 2008 [45]	EXP: Telephone counselling CON: Waitlist control	n=130 EXP= 70 47.5 years CON= 60 45 years	EXP DO 6/70 (9%) CON DO 1/60 (2%) Adherence 53% received <2 hours telephone contact Adverse events NR MS relapses NR	EDSS ≤ 5.5 MS Type All	12 weeks 60-90 minutes face-to-face meeting, approx. 30mins telephone in weeks 1, 2, 4, 8, & 12	1 face-to-face meeting (motivational interviewing and goal setting), 5 telephone counselling sessions covering exercise, fatigue, communication and/or social support, anxiety and/or stress management, reducing alcohol or drug use
Ennis et al. 2006 [55]	EXP: Health promotion education programme CON: Usual care	n=64 EXP= 34 45(9) years CON= 30 46(8) years	EXP DO 2/34 (6%) CON DO 0/30 (0%) Adherence NR No adverse events MS relapses NR	EDSS 1-7 MS Type All	8 weeks 3 hour sessions/week	Group session topics covered: exercise & PA, lifestyle adjustment/ fatigue management, stress management, nutritional awareness, responsible health practices

Stuifbergen et al 2003 [56]	EXP: Lifestyle change CON: Waitlist control	n=142 women only Analysed 113 45.8(10.1) years EXP= 56 Allocated (n=76) CON= 57 Allocated (n=66)	EXP DO 5/61 (8%) CON DO 3/60 (5%) Adherence 75% Adverse events NR MS relapses NR	EXP ISS 14.9±24.1 CON ISS 16.4±8.6 MS Type RRMS	5 months 90 minutes session/week, 8 weeks, bimonthly telephone support, 12 weeks	Group session topics covered: lifestyle adjustment, exercise & PA for fun, endurance, strength, healthy eating, stress management, intimacy & sexuality, women's health. Telephone: support goal attainment & self-efficacy
Mostert & Kesselring 2002 [32]	EXP: Exercise training CON: Usual care	n=26 EXP= 13 45.2(8.7) years A-CON= 13 43.9(13.9) years	EXP DO 4/17 (24%) A-CON 5/18 (28%) Adherence 65% Adverse events (n=2) MS relapses NR	EXP EDSS 4.6±1.2 CON EDSS 4.5±1.9 MS Type All	4 weeks, 30 minute/session, 5 times/week	30 minute bicycle training at aerobic threshold Actual mean exercise training time-327 minute over 14 training sessions within 3-4 weeks

Abbreviations: A-CON: Attention-Control Group; APDDS: Adapted Patient Determined Disease Steps; BT: Balance Training CON: Control Group; BRPE: Borg Rating of Perceived Exertion; CT: Continuous Training; DO: Drop outs; ET: Endurance Training; EXP: Experimental Group; EDSS: Expanded Disability Status Scale; HR: Heart Rate; ISS: Incapacity Status Scale (max score 64); IT: Interval Training; LL: Lower Limb; MPS: Mobility Performance Scale; MS: Multiple Sclerosis; MSFC: Multiple Sclerosis Functional Composite; n: number; NR: Not Reported; pwMS: people with Multiple Sclerosis; PA: Physical Activity; PDDS: Patient Determined Disease Steps; RM: Repetition Maximum; RPE: Rate of Perceived Exertion; RT: Resistance Training; RRMS: Relapsing Remitting Multiple Sclerosis; S: Static Stretching; SCT: Social Cognitive Theory; SPMS: Secondary Progressive Multiple Sclerosis; UL: Upper Limb.

*median

ϒ a score close to zero indicates that participants are comparable to the population with MS

Table 3. Evidence table for included randomised controlled studies.

Study	PO/SO	PA/SB instrument and cut points (units)	Baseline PA level	Post intervention PA level	Time effects on PA level	Time x Group interaction on PA level	Beneficial effects of intervention
Thomas et al. 2017 [54]	Leisure-time PA, HADS, EQ-5D, MSIS, FSI, SF-36, SCI-ESES, MSSE, 2MWT, Step test, Steady Stance test, i-TUG, Gait Stride-time Rhythmicity, Static Posturography, 9HPT	GLTEQ (arbitrary unit)	Leisure-time PA EXP 11.1(12.4) CON 7.9(11.4)	Leisure-time PA EXP 22.5(16.4) CON 11.2(9.8) 12 months Leisure-time PA EXP 28.0(24.6)	Effect size 0.70	NR	↑ HADS ↑ MSIS ↑ SF-36 ↑ SCI-ESES ↑ MSSE
Motl et al. 2017 [46]	PO: Leisure-time PA, MVPA SO: MFIS, FSS, HADS, SF-MPQ, MSWS	GLTEQ (arbitrary unit) Actigraph GT3X+ (MVPA minutes)	Leisure-time PA EXP 10.8(14.0) CON 12.7(14.8) MVPA EXP 13.9(9.2) CON 17.5(18.3)	Leisure-time PA EXP 27.2(4.5) CON 14.1(4.7) MVPA EXP 28.8(5.0) CON 20.2(5.2)	NR	↑ Leisure-time PA — MVPA	↑ MFIS ↑ MSWS
Hugos et al. 2017 [58]	PO: MFIS SO: frequency/intensity of CV exercise, frequency of strength exercise, frequency of flexibility exercise, MSSE, PSQI, BDI	RAPA (arbitrary unit)	CV EXP 34% CON 39% Strength EXP 49% CON 49% Flexibility EXP 67% CON 67%	CV EXP 40% CON 32% Strength EXP 51% CON 51% Flexibility EXP 69% CON 62% 3 month CV EXP 36% CON 32% Strength EXP 52% CON 50% Flexibility EXP 70% CON 70%	— CV — Strength — Flexibility 3 month — CV — Strength — Flexibility 6 month — CV — Strength — Flexibility	— CV — Strength — Flexibility 3 month — CV — Strength — Flexibility 6 month — CV — Strength — Flexibility	↑ MSSE 3 month NS 6 month ↑ PSQI

				6 month CV EXP 33% CON 34% Strength EXP 47% CON 52% Flexibility EXP 66% CON 64%			
Coote et al. 2017 [52]	SO: Total PA, Leisure-time PA, HADS, SDMT, MSIS, MFIS, ESES, EGS, MOEES, SPS, EBBE [μ]	SenseWear arm band (steps/day, EE/day) GLTEQ (unknown unit)	Steps/day EXP 6098(2363) CON 7223(2695) EE/day EXP 1909(300) CON 2032(383) Leisure-time PA EXP 3.0(6.2) CON 2.8(9.1)	Steps/day EXP 6108(3305) CON 7582(2372) EE/day EXP 1909(372) CON 1897(427) Leisure-time PA EXP 13.8(11.7) CON 16.1(21.1) 6 month Steps/day EXP 6429(2448) CON 7397(2612) EE/day EXP 1866(408) CON 1852(368) Leisure-time PA EXP 15.2(13.9) CON 16.0(16.7) 9 month Steps/day EXP 6558(3059) CON 7450(3100) EE/day EXP 1823(348) CON 1900(355) Leisure-time PA EXP 15.7(14.8) CON 15.0(20.9)	↑ Leisure-time PA — Steps/day — EE 6 month ↑ Leisure-time PA — Steps/day — EE 9 month ↑ Leisure-time PA — Steps/day — EE	— Leisure-time PA — Steps/day — EE 6 month — Leisure-time PA — Steps/day — EE 9 month — Leisure-time PA — Steps/day — EE	NS 6 month NS 9 month NS
Hayes et al. 2017 [53]	PO: 6MWT	GLTEQ (unknown unit)	As above	As above	As above	As above	↑ 6MWT ↑ MSWS

	SO: Leisure-time PA, MSWS, TUG, 5STS, MCAFT						↑ TUG ↑ 5STS 6 month ↑ 6MWT ↑ MSWS ↑ TUG 9 month ↑ 6MWT ↑ MSWS ↑ TUG
Learmonth et al. 2017 [47]	PO: Leisure-time PA SO: MVPA, MSWS, ABC, FSS, LLFDI, HADS, MPQ, MSIS, LMSQoL, ESES, EGSPS, MOEES, SPS, EBBE	GLTEQ (unknown unit) Actigraph GT3X (MVPA minutes)	GLTEQ EXP 20.38(15.64) CON 19.64(20.78) MVPA EXP 25.54(18.05) CON 21.05(18.78)	GLTEQ EXP 29.36(19.68) CON 16.85(19.54) MVPA EXP 26.64(15.49) CON 22.55(22.46)	NR	↑ Leisure-time PA — MVPA	↑ EGSPS- goal ↑ EBBE-barrier
Dashti et al. 2016 [33]	Health Promoting Lifestyle	HPLP-II (Total PA- PA subscale) [Scored 8-32]	EXP 15.2(3.9) CON 15.4(3.9)	EXP 16.2(2.2) CON 14.5(2.2) 1 month EXP 16.1(2.5) CON 14.6(2.5)	NR	↑ Total PA 1 month ↑ Total PA	1 week & 1 month ↑Nutrition ↑Stress-management ↑Interpersonal relationships ↑Responsibility
Tallner et al. 2016 [30]	PO: HAQUAMS SO: Sport PA, Strength, aerobic capacity, FVC, VO_2peak, PEFR, WEIMuS	BAECKE questionnaire (unknown unit)	EXP Sport PA 2.30(2.47) CON Sport PA 2.10(2.43)	EXP Sport PA 3.24(2.73) CON Sport PA 1.90(2.39) 6 month EXP 3.36 (2.33)	↑ Sport PA 6 month — Sport PA	↑ Sport PA	↑ PEFR ↑ Knee strength ↑ Trunk strength
Turner et al. 2016 [34]	PO: MFIS SO: Leisure-time PA, PHQ-9, MSRSC	GLTEQ (MET/week)	EXP 16.37(3.54)$^{\alpha}$ A-CON 14.79(3.37)$^{\alpha}$	3 month EXP 29.68(3.72)$^{\alpha}$ A-CON 19.74(3.54)$^{\alpha}$ 6 month EXP 31.06(3.19)$^{\alpha}$ A-CON 15.43(3.04) $^{\alpha}$	— Leisure-time PA	3 month ↑ Leisure-time PA 6 months ↑ Leisure-time PA	3 month ↑ Fatigue ↑ Depression ↑ MSRSC 6month ↑ Fatigue

McAuley et al. 2015 [29]	Leisure-time PA, SPPB, MSIS, Upper body strength & endurance, Back Scratch Test, Sit and Reach Test, Grip Strength, SLS, Sitting Time Questionnaire [μ]	GLTEQ (Unknown unit, MVPA) Sitting Time Questionnaire (minute/day)	Leisure-time PA EXP 8.47(1.86)[α] A-CON 6.85(1.82)[α] MVPA EXP 2.72(1.44)[α] A-CON 2.72(1.41)[α] ST (weekdays) EXP 659.67(52.17)[α] A-CON 77.92(51.02)[α] ST (weekend) EXP 676.27(71.11)[α] A-CON 713.78(69.55)[α]	Leisure-time PA EXP 21.54(3.03) A-CON 12.61(2.86) MVPA EXP 10.62(2.29) A-CON 4.66(2.24) ST (weekdays) EXP 621.16(64.93) A-CON 788.02(63.50) ST (weekend) EXP 673.43(70.06) A-CON 743.68(68.52)	↑ Leisure-time PA ↑ MVPA — SB (weekdays) — SB (weekend)	NR	↑ Back Scratch Test
Rice et al. 2015 [35]	Total PA, Wheelchair propulsion efficiency, Upper extremity muscle strength, FSS [μ]	Actigraph GT3X (activity counts)	EXP 980,428.9(547,676.5) CON 923,499.3(475,384.4)	EXP 1,111,080.1(510,500.4) CON 979,454.1(639,999.5)	NR	— Total PA	↑ Braking torque ↑ Pectoralis major strength
Suh et al. 2015 [36]	PO: Leisure-time PA SO: ESES, MOEES, LLFDI, EGS, SSES	GLTEQ (Score 0-119)	EXP 19.1(14.8) A-CON 22.7(19.4)	EXP 27.4(20.6) A-CON 19.1(14.8)	↑ Leisure-time PA	↑ Leisure-time PA	↑ EGS ↑ ESES
Wens et al. 2015 [28]	PO: Muscle fibre CSA and proportion SO: Total PA, Isometric muscle strength, VO_2 max, EV, RER, HR, Lean body mass, Waist-Hip Ratio	PASIPD (MET*hour/week)	IT 25.8(6.6) CT 14.7(2.7) CON 16.0(2.6)	IT 37.6(7.2) CT 23.9(4.4) CON 15.8(3.7)	IT ↑ Total PA CT ↑ Total PA	IT ↑ Total PA CT ↑ Total PA	IT ↑CSA ↑Muscle fibre type II and IIa ↑Muscle strength ↑ VO2 max ↑ Lean body mass CT ↑CSA ↑Muscle fibre type I ↑Muscle strength
Carter et al. 2014 [48]	PO: Leisure-time PA, step count SO: MFIS, MSQoL-	GLTEQ (MET/week) Actigraph (GT2M	Leisure-time PA EXP 20.3(21.9) CON 17.5(14.8) Steps/day	12 week difference between groups Leisure-time PA ↑9.6 Steps/day ↑688.5	12 weeks ↑ Leisure-time PA ↑ Steps/day	NR	12 weeks ↑ MSQoL-54 ↑ MFIS

	54, MSFC, 6MWT, EDSS	accelerometer) (Steps/day)	EXP 4,488(2,251) CON 4,695(2,711)	9 month difference between groups Leisure-time PA ↑6.9 Steps/day ↓18	9 months follow up — Leisure-time PA — Steps/day		
Pilutti et al. 2014 [37]	PO: FSS SO: Leisure-time PA, MVPA, MFIS, HADS, MPQ, PSQI, MSIS	GLTEQ (Score 0-119) Actigraph (GT3X accelerometer) (MVPA minute/day)	Leisure-time PA EXP 15.6(19.9) CON 17.2(15.2) MVPA EXP 17(22.4) CON 16.2(17.7)	Leisure-time PA EXP 27.2(3.0)[β] CON 13.0(3.0)[β] MVPA EXP 19.5(2.3)[β] CON 13.8(2.2)[β]	↑ Leisure-time PA — MVPA	NR	↑ FSS ↑ MFIS-physical ↑ HADS-D ↑ HADS-A ↑ MSIS- psych
Pilutti et al. 2014 [38]	PO: BMI, BMC, BMD SO: Leisure-time PA, MVPA	GLTEQ (Score 0-119) Actigraph (GT3X accelerometer) (MVPA minute/day)	As above	NR[δ]	As above	NR	↑ BMC ↑ BMD
Sandroff et al. 2014 [39]	PO: SDMT SO: Total PA, 6MWT,	IPAQ (Total score 0-117)	EXP 17.44(20.8) CON 22.83(18.8)	EXP 29.66(20.7) CON 19.31(17.0)	NR	↑ Total PA	↑ 6MWT
Klaren et al. 2014 [40]	PO: SB	IPAQ (minutes/day)	EXP 429.2(201.2)[ϒ] CON 528.2(200.7)[ϒ]	EXP 405.4(211.6)[ϒ] CON 534.3(211.4)[ϒ]	NR	↑ SB	NR
Plow et al. 2014 [49]	PO: Leisure-time PA, Total PA SO: SF-12, MSIS, SMSS, 6MWT, Sit and Reach Test, Back Scratch Test, Chair Stands, Arm Curls, 8ft Up and Go Test	GLTEQ (Unknown units) PADS-R (Unknown units)	Leisure-time PA EXP 14.36(11.92) CON 16.22(17.29) Total PA EXP 0.01(0.83) CON 0.36(1.09)	Leisure-time PA EXP 33.07(21.42) CON 21.00(18.53) Total PA EXP 0.98(0.76) CON 0.14(1.13) 6 month Leisure-time PA EXP 30.54(13.23) Total PA EXP 0.77(0.74)	6 month ↑ Total PA ↑ Leisure-time PA	12 week ↑ Total PA ↑ Leisure-time PA	↑ SMSS ↑ Chair Stands ↑ Arm Curls
Bombardier et al. 2013 [42]	PO: HAM-D SO: Total PA, SCID, SCL-20, PANAS,	7-Day PAR (kcal/kg/week)	EXP 223.5(8.2) CON 222.6(6.9)	EXP 228.5(9.9) CON 224(9.2) 6 months	↑ Total PA	NR	↑ HAM-D ↑ SCL-20 ↑ SCID ↑ PANAS-

	MSRSC			EXP 228.8(9.1)			positive affect ↑ PANAS-negative affect ↑ MSRSC
Kratz et al. 2014 [41]	PO: HAM-D SO: Total PA, SCID, SCL-20, PANAS, MSRSC,	7-Day PAR (minute/week)	EXP 16.7(31.7) CON 35.7(43.8)	NR	↑ Total PA	NR	↑ PANAS-positive affect ↑ PANAS-negative affect
Carter et al. 2013 [50]	Leisure-time PA [μ], BMI, waist:hip ratio, Aerobic capacity, T25FW, MSQoL54	GLTEQ (Unknown units)	EXP 14.7(14.9) CON 13.2(12.0)	EXP 14.7(14.4) CON 13.3(11.8) 6 month EXP 17.8(12.5) CON 14.4(8.4)	═ Leisure-time PA 6 month ═ Leisure-time PA	NR	↑ MSQoL54 physical
Dlugonski et al. 2012 [43]	PO: Leisure-time PA SO: MSWS, MSIS,	GLTEQ (MET/minute/week)	EXP 13.6(11.6) CON 16.1(14.2)	EXP 28.2(15.6) CON 15.4(13.9) 6 month EXP 26.9(16.2) CON 14.5(11.4)	NR	↑ Leisure-time PA 6 months ↑ Leisure-time PA	NS
Learmonth et al. 2012 [31]	PO: T25FW SO: Total PA, BMI, 6MWT, BBS, TUG, Strength, ABC, FSS, HADS, LMSQoL, GAS	PhoneFITT questionnaire (arbitrary unit)	EXP 53.3 (20.6) CON 54.6(26.6)	8 week EXP 69.7(23.6) CON 38.3(23.1) 12 week EXP 78.2(35.5) CON 54.6(16.7)	8 week ↑ Total PA 12 week (post intervention) ↑ Total PA	8 week ↑Total PA 12 week (post intervention) ↑ Total PA	↑ ABC
Motl et al. 2011 [44]	PO: Leisure-time PA SO: ESES, MOEES, LLFDI, EGS	GLTEQ MET/minute/week	EXP 13.8(15.2) CON 11.7(16.3)	EXP 24.7(18.8) CON 12.4(14.2)	↑ Leisure-time PA	↑ Leisure-time PA	↑ EGS
Plow et al. 2009 [51]	PO: SF-36, MFIS, MHI SO: PA frequency, Physical assessment	HPLP-II (Total PA- PA subscale) (Unknown unit)	NR	Effect sizes EXP1 0.93 EXP2 0.65	Both groups ↑ Total PA 8 weeks Both groups ↑ Total PA	═ Total PA	Both groups ↑ MFIS ↑Resting HR ↑Waist circumference ↑Body fat % ↑Strength EXP1 ↑ MFIS ↑ physical health

							EXP 2 ↑ mental health
Bombardier et al. 2008 [45]	PO: Health promoting Lifestyle SO: MFIS, SF-36, MSSS, CHART, Lower limb strength, walking speed, MSFC	HPLP-II (Total PA- PA subscale) (unknown unit)	NR	Change scores EXP 0.4 [0-0.9] CON 0.0 [-0.3-0.3]	NR	↑Total PA	↑ HPLP-II ↑ MFIS ↑ SF-36 mental
Ennis et al. 2006 [55]	PO: Health promoting Lifestyle SO: SRAHP, SF-36	HPLP-II (Total PA- PA subscale) [Scored 8-32]	EXP 12.6(4.4) CON 13.1(3.7)	EXP 19.1(5.3) CON 13.3(4.1)	↑ Total PA	NR	↑ HPLP-II ↑ SF-36 ↑ SRAHP
Stuifbergen et al 2003 [56]	PO: Health promoting Lifestyle SO: ISS, BHPADPS, PRQ-85, SRAHP, SF-36	HPLP-II (Total PA- PA subscale) [Scored 8-32]	EXP 16.8(5.9) CON 14.9(5.1)	8 week EXP 19.0(6.1) CON 15.6(4.6) 5 month EXP 20.0(5.7) CON 15.2(5.6) 8 month EXP 20.0(5.7) CON 16.0(5.1)	NR	8 week ↑ Total PA 5 month ↑ Total PA 8 month ↑ Total PA	↑ HPLP-II ↑ SRAHP
Mostert & Kesselring 2002 [32]	Sport PA, Work PA, Leisure PA, Aerobic fitness, SF-36, FSS [μ]	BAECKE Activity Questionnaire [Scored 0-5]	Work PA EXP 2.7(0.7) A-CON 2.5(0.9) Sport PA EXP 1.7(0.7) A-CON 1.8(0.4) Leisure PA EXP 2.4(0.6) A-CON 2.3(0.7)	Work PA EXP 2.6(0.6) A-CON 2.7(0.9) Sport PA EXP 2.0(0.4) A-CON 1.7(0.4) Leisure PA EXP 2.5(0.8) A-CON 2.4(0.8)	↑ Sport PA — Work PA — Leisure PA	NR	↑ FVC ↑ PEFR ↑ SF-36- vitality ↑ SF36- social

Abbreviations: A-CON: Attention-Control Group; ABC: Activities-specific Balance Confidence; BBS: Berg Balance Scale; BDI: Beck Depression Inventory; BHPADPS: Barriers to Health Promoting Activities for Disabled Persons Scale; BMC: Bone Mineral Content; BMD: Bone Mineral Density; BMI: Body Mass Index; CHART: Craig Handicap Assessment and Reporting Technique; CON: Control Group; CSA: Cross-Sectional Area; CT: Continuous Training; CV: Cardiovascular; EBBE: Exercise Benefits and Barriers Scale; EDSS: Expanded Disability Status Scale; EE: Energy Expenditure; EGS: Exercise Goal setting Scale; EGSPS: Exercise Goal Setting and Planning Scale; ESES: Exercise Self-Efficacy Scale; EQ-5D: EuroQoL-5 Dimensions; EV: Expiratory Volume; EXP: Experimental Group; FSI: Fatigue Severity Index; FSS: Fatigue Severity Scale; FVC: Forced Vital Capacity; GAS: Goal Attainment Scale; GLTEQ: Godin Leisure Time Exercise Questionnaire; HADS: Hospital Anxiety and Depression Scale; HADS-A: Hospital Anxiety and Depression Scale- Anxiety

Subscale; HADS-D: Hospital Anxiety and Depression Scale- Depression Subscale; HAM-D: Hamilton Depression Rating Scale; HAQUAMS: Hamburg Quality of Life Questionnaire for Multiple Sclerosis; HPLP-II: Health Promoting Lifestyle Profile-II; HR: Heart Rate; IPAQ: International Physical Activity Questionnaire; ISS: Incapacity Status Sale; IT: Interval Training; i-TUG: Instrumental Timed Up and Go; LLFDI: Late-life Function and Disability Instrument; LMSQoL: Leeds Multiple Sclerosis Quality of Life; MCAFT: Modified Canadian Aerobic Fitness Test; MET: Metabolic equivalent; MFIS: Modified Fatigue Impact Scale; MHI: Mental Health Inventory; MOEES: Multidimensional Outcome Expectancies for Exercise Scale; MPQ: Short-Form McGill Pain Questionnaire; MSFC: Multiple Sclerosis Functional Composite; MSIS: MS Impact Scale; MSIS-physical: MS Impact Scale-physical subscale; MSIS-psych: MS Impact Scale-psychological subscale; ; MSQoL-54: MS Quality of Life 54 Scale; MSRSC: MS Related Symptom Checklist; MSSE: Multiple Sclerosis Self-Efficacy Scale; MSSS: Modified Social Support Scale; MSWS: Multiple Sclerosis Walking Scale; MVPA: Moderate-Vigorous Physical Activity; MVV: Maximum Voluntary Ventilation; NR: Not Reported; NS: No significant changes; PA: Physical Activity; PADS-R: Physical Activity and Disability Survey-revised; PANAS: Positive and Negative Affect Scale; PASIPD: Physical Activity Scale for Individuals with Physical Disabilities; PEFR: Peak Expiratory Flow Rate; PHQ-9: Patient Health Questionnaire; PO: Primary Outcome; PRQ-85: Personal Resource Questionnaire; PSQI: Pittsburgh Sleep Quality Index; RAPA: Rapid Assessment of Physical Activity; RER: Respiratory Exchange Ratio; SB: Sedentary Behaviour; SCID: Structured Clinical Interview for DSM-IV; SCI-ESES: Spinal Cord Injury Exercise Self-Efficacy Scale; SDMT: Symbol Digit Modalities Test; SF-12: Short Form 12 Questionnaire; SF-36: Short-Form 36 Health Questionnaire; SF-MPQ: Sort-Form McGill Pain Questionnaire; SLS: Satisfaction with Life Scale; SCL-20: Hopkins Symptom Checklist; SMSS: Symptoms of MS Scale; SO: Secondary Outcome; SPPB: Short Physical Performance Battery; SPS: Social Provisions Scale; SRAHP: Self Rated Abilities for Health Practices; SSES: Social Support and Exercise Survey; TUG: Timed Up and Go; T25FW: Timed 25ft Walk; WEIMuS: Würzburg Fatigue Scale for Multiple Sclerosis; 2MWT: Two Minute Walk Test; 5STS: Five Times Sit To Stand; 6MWT: 6 Minute Walk Test; 7-Day PAR: 7-Day Physical Activity Recall; 9HPT: Nine-Hole Peg Test.

↑ - indicates significant improvement in outcome, ▬ - indicates no significant improvement in outcome

$^{\Upsilon}$ Adjusted Mean(SD)

$^{\alpha}$ Mean(SE)

$^{\mu}$ Primary outcome not defined

$^{\beta}$ Estimated marginal mean(SE)

$^{\delta}$ Reported in another article